BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

REMARKS

Claims 1-14 are pending in this application. Claims 4-11, 13, and 14 have been withdrawn from consideration as being drawn to the non-elected invention. Claims 1-3, and 12 stand rejected. None of the claims stand objected to. The Applicants herein amend the specification to address an objection raised by the Examiner, which is discussed further below, as well as to correct an obvious typographical error. The Applicants herein cancel Claims 1-3 without prejudice or disclaimer to the subject matter contained therein. For the purpose of clarifying the instantly claimed invention, the Applicants herein amend Claim 12, and add new Claims 15-23. Claim 12, as amended, finds support in the instant specification at page 9, line 26 through page 10, line 3, as well as page 30, line 28 through page 31, line 4. New Claims 15-23 find support at pages 4-5, 15, 24, 27-28, and 30-31 of the instant specification. New Claims 15-23 are directed to the subject matter of elected Group I. None of these amendments to the specification or claims introduce new matter into the application. In view of the following amendment and response, the Applicants believe the claims presented herein are allowable. Reconsideration is respectfully requested.

The Applicants thank the Examiner for the courtesy he showed to co-inventor, Dr. Shelton, and the Applicants' attorney, Ms. Hecht, during the interview on 22 October 2003. During this interview, Examiner Paras, Dr. Shelton, and Ms. Hecht discussed the various rejections of Claims 1-3 and 12 under 35 U.S.C. § 112, first paragraph. Specifically, Dr. Shelton and Ms. Hecht addressed Examiner Paras' concerns raised in the Office Action, and they explained to Examiner Paras how this platform screening technology works.

OBJECTIONS TO THE SPECIFICATION

The Examiner objects to the disclosure of the specification at page 15, lines 32-33 because it contains an embedded hyperlink. The Examiner has requested appropriate

correction, per MPEP § 608.01(a). At the time the instant application was filed, the abstract within this cited hyperlink was not yet available in hard copy. Since then, the full paper that arose from the cited abstract, Tobin, *et al.*, *Neuron*, 35: 307-318 (2002) (copy enclosed herewith and cited in a PTO Form 1449), has published. Accordingly, the Applicants herein replace the citation to the hyperlink at page 15, lines 32-33 with the a citation to the summary of Tobin, *et al.* This amendment raises no issue of new matter.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-3, and 12 stand rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the written description requirement. The Examiner maintains that the claims allegedly contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. In the instant specification, the Applicants disclose the nucleotide sequences that encode five h7MRs (GPR18, GPR7, HCEPR, AXOR35, and Octoray). On page 4 of the Office Action, the Examiner argues, "There is no evidence on the record of a relationship between the structure of any h7TMR cDNA and the 7TMR cDNAs embraced by the claims that would provide any reliable information about the structure of other 7TMR cDNAs within the genus."

The Applicants respectfully traverse this rejection. As they herein cancel Claims 1-3 without prejudice or disclaimer, the instantly pending claims relate only to screening methods, not transgenic animals or methods of making transgenic animals. The Applicants traverse this rejection of Claim 12, as amended, and new Claims 15-23.

Contrary to the Examiner's arguments, the Applicants respectfully submit that a structural link exists between the five disclosed h7TMRs and the entire class of h7TMRs that comprise the genus of the instant claims. Indeed, the scientific literature supports such a link.

For example, Stadel, *et al.*, *Trends Pharmacol. Sci.* 18(11): 430-437 (1997) (copy enclosed and submitted with PTO Form 1449), explain: "The members of the GPCR superfamily are related both structurally and functionally. The signature motif of these receptors is seven distinct hydrophobic domains, each of which is 20-30 amino acids long and which are linked by hydrophilic amino acids of varied length. . . Therefore, these receptors are often referred to as seven transmembrane (or 7TM) receptors." Drawing a similar conclusion, Karnik, *et al, Trends in Endocrinology and Metabolisum* 14(9): 431-437 (2003) (copy enclosed), explain: "The conservation of the 7TM motif might indicate that the mechanism of activation and G-protein-coupling in GPCR signal transduction is preserved."

In fact, human 7TMRs share so many common structural features that bioinformaticians can readily identify them based upon very little sequence information. Stadel, *et al.*, *supra*, at page 434, describe this process by stating: "Through both traditional molecular cloning techniques and, more recently, mass sequencing of expressed sequence tags (ESTs) from cDNA libraries, it is now possible to identify GPCRs through computational or bioinformatic methodologies." Therefore, the Applicants submit that the description of the 5 7TMRs in the instant specification sufficiently apprises the skilled artisan of the subject matter of the instant screening claims. To satisfy the written description requirement, the subject matter of the claim need not be described literally in the specification. *See, e.g., In re Lukach*, 169 U.S.P.Q. 795, 796 (C.C.P.A. 1971). Rather, an applicant can fulfill this requirement by conveying clearly to the skilled artisan that the applicant invented the claimed subject matter. *See, e.g., In re Wertheim*, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976).

While the Examiner cites *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q.2d 1398, 1404-05 (Fed. Cir. 1998) to support this written description rejection, the Applicants respectfully assert that *Lilly* does not apply to the instant application. UC's claims at issue in

Lilly recited "mammalian insulin cDNA" and "vertebrate insulin cDNA", although the patents-in-suit only disclosed rat insulin cDNA. *Id.* at 1401. In limiting UC's patents to cover only rat insulin cDNA, the court held that the mere disclosure of rat insulin cDNA failed to support broad claims to mammalian and vertebrate insulin cDNA. *Id.* at 1406. In direct contrast to the claims in *Lilly*, all of the instantly pending claims relate only to screening methods. Indeed, Applicants are not claiming h7TMR proteins or cDNA encoding h7TMRs. As discussed above, the skilled artisans can easily identify h7TMRs to employ in the instant screening methods, and then create a transgenic *C. elegans* that express the desired h7TMR in its sensory neurons. For that reason, the Applicants need not describe every h7TMR that the instantly pending claims embrace. In view of the above arguments and amendments, the Applicants submit that Claims 12 and 15-23 satisfy the written description requirement.

Claims 1-3, and 12 also stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. The Examiner maintains that the claims contain subject matter allegedly not described in the specification in such as way as to enable one skilled in the art to make and/or use the invention. Specifically, he makes the following two distinct enablement arguments. First, the Examiner alleges that the specification fails to correlate phenotypes other than the egg laying defect (egl) with expression of h7TMRs. Essentially, he bases this ground of rejection on phenotypic unpredictability. Second, the Examiner argues that the specification fails to provide guidance that correlates the disclosed phenotypes with known diseases or disorders that can be treated. These rejections are moot for Claims 1-3, which the Applicants herein cancel. The Applicants, however, traverse these rejections of Claim 12, as amended, as well as new Claims 15-23.

Responding to the first enablement rejection, the Applicants assert that, to practice the claimed invention without undue experimentation, the skilled artisan need not be able to correlate a phenotype with the expression of a specific h7TMR. Practice of the claimed screening methods merely requires that the transgenic *C. elegans* that expresses a h7TMR exhibits **a** known phenotype. As disclosed at page 12, lines 21-28 of the specification, the Applicants define "known phenotype" to include 24 phenotypes. The scientific literature supports the existence of all 24 of these phenotypes in *C. elegans*. *See, e.g.,* Fraser, *et al., Nature* 408: 325-330 (2000) (copy enclosed), for the disclosure of the following disclosed phenotypes: dumpy (Dpy), long body (Lon), molt defect (Mlt), sterile (Ste), sick (Sck), body morphology defect (Bmd), slow growth (Gro), egg-laying defect (Egl), larval arrest (Lva), protruding vulva (Pvl), multiple vulva (Muv), sterile progeny (Stp), small (Sma), clear (Clr), roller (Rol), larval lethal (Lvl), uncoordinated (Unc), high incidence of males (Him), blistered (Bli), and embryonic lethal (Emb). *See* Jorgensen, *et al.*, *Nature*, Vol. 3: 356-369 (2002) (copy enclosed), for disclosure of the phenotypes lethal (Let) and vulvaless (Vul).

Through inadvertent error, and without deceptive intent, the Applicants listed the larval lethal phenotype twice in the instant specification, once associated with the abbreviation Let, and once with the abbreviation Lvl. Applicants have informed the undersigned that Lvl is the correct abbreviation for this phenotype. Let simply refers to lethal. The Applicants herein amend the specification to correct this inadvertent error.

Lastly, there are two phenotypes disclosed in the specification, hyperactive movement (Hpr) and paralyzed (Prl), which to not exactly match those in the scientific literature. However, although the Hpr and Prl abbreviations do not appear in the literature, the Applicants have informed the undersigned that Kamath, *et al.*, *Nature* 421: 231-237 (2003) (copy enclosed) support these two phenotypes. Kamath, *et al.* disclose the Hya and Prz phenotypes, which are synonymous in the art with the Hpr and Prl phenotypes listed by the

Applicants in the instant specification. Finally, there is one phenotype that the Applicants list, exploded (Exp), for which Kamath, *et al.* uses a different phenotype and abbreviation. The Applicants have informed the undersigned that the ruptured (Rup) phenotype in Kamath, *et al.* is synonymous in the art with the Applicants listed phenotype, exploded (Exp). In summary, the Applicants submit that those of skill in the art would recognize all of the 24 listed phenotypes in that *C. elegans* exhibits.

While the Applicants demonstrate only the egg laying (Egl) phenotype in the instant specification, they assert that the inventive screening methods will work with any of the other 23 known phenotypes. Skilled artisans can routinely and quickly score each of these known phenotypes. As long as the transgenic worm expresses one of the 24 known phenotypes, it can be utilized in the claimed screening methods.

Turning now to the second enablement rejection, the Applicants respectfully clarified with the Examiner during the interview that the claimed methods are screening methods to identify compounds that may be useful therapeutics to treat a variety of human diseases. Therefore, the inventive methods are not method of treatment claims that are intended to directly treat human disease. In addition, the transgenic worms of the claims do not serve as disease models. Accordingly, the Applicants submit that, in order to practice the claimed screening methods, the skilled artisan need not yet know the specific disease that the identified compound may ultimately treat. Indeed, the phenotype that the transgenic worm exhibits has no bearing on the ultimate disease that the identified antagonist will treat. Therefore, the Applicants submit that the law does not require them to correlate each phenotype with a disease.

While the Examiner contends that Link, *et al., Mechanisms of Aging and Development*, 122: 1639-1649 (2001), supports this first enablement rejection, the Applicants respectfully disagree. First, Link, *et al.* employs the all of the animals described as disease

models. As mentioned above, the *C. elegans* that the Applicants employ serve as vehicles in screening methods, rather than disease models. Second, in each of the three *C. elegans* models that Link, *et al.* test, the animals exhibited a phenotype. *See* Table 1, page 1641. For these reasons, the Applicants assert that Link, *et al.* actually supports their contention that one of skill in the art can engineer a *C. elegans* to exhibit a known phenotype. The phenotypic unpredictability referred to by the Examiner in Link, *et al.* relates to animals other than *C. elegans*, such as *Drosophila*.

The Applicants respectfully submit that in view of the forgoing remarks and the claims as amended, the Applicants have overcome the Examiner's rejection under 35 U.S.C. §112, first paragraph, and the rejection should be withdrawn.

The Applicants reserve the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the cancelled claims, the claims as originally filed, and any other claims supported by the specification. The Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited. If it would expedite the prosecution of this application, the Examiner is invited to confer with the Applicants' undersigned attorney.

Respectfully submitted,

Elizabeth J. Hecht
Attorney for Applicants
Registration No. 41,824

GlaxoSmithKline
Corporate Intellectual Property - UW2220
P.O. Box 1539
King of Prussia, PA 19406-0939
Phone (610) 270-5009
Facsimile (610) 270-5090
N:\EJH\APPLNS\P51176\roa1.doc